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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,683	08/07/2001	Heinrich Decker	38005-0152	9675

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 11/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,683	DECKER, HEINRICH	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 34-37 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 9-2-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 36 is drawn to a process of preparing acarbose comprising few steps, wherein the first step is eliminating or altering endogenous acarbose-synthesizing genes in a transformed cell that has the capacity of producing acarbose naturally. This step is followed by culturing and isolating acarbose which is produced by the activity of remaining genes selected from a group of nucleotides of SEQ ID NO:7. It is not clear to the Examiner as to how one skilled in the art would be able to select the "remaining genes" if there is no information as to which gene is eliminated in the first step. Next, claim 36 recites in the first step that the host cell produces acarbose naturally, acarbose synthesizing is eliminated or altered and the host cell is transformed. The following are not clear to the Examiner. It is not clear to the Examiner as to which are the genes (or nucleotides of SEQ ID NO:7) that are eliminated or altered and what is

the scope of the term "altered" (i.e., gene activity is reduced or enhanced or totally eliminated), and what is the host cell transformed with? Therefore claims 36 and 37 remain unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of preparing acarbose comprising the steps of transforming a host cell (either before or after eliminating native acarbose synthesizing genes) with a suitable expression vector comprising SEQ ID NO:7 (comprising all the sequences essential for encoding acarbose synthesizing enzymes), followed by culturing the transformant under conditions such that the transformed genes are expressed and acarbose is synthesized followed by isolation of the accumulated acarbose, does not reasonably provide enablement for a method of producing acarbose by simply expressing one or more fragments of SEQ ID NO:7 (as in claim 34) or for a process comprising isolating acarbose from naturally-acarbose-producing host cells in which the native acarbose synthesizing genes are all eliminated (as in claims 36-37) or altered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 34-37 are so broad as to encompass a method of making acarbose by transforming a host cell or expressing either the full length SEQ D NO:7 or one or more specific fragments of SEQ ID NO:7 and a method of making acarbose wherein the native acarbose genes are eliminated or altered. The scope of the claims is not commensurate with the enablement provided by the disclosure. It appears that the entire sequence of SEQ ID NO:7 is required to encode all the enzymes involved in the synthesis of acarbose. Furthermore, applicants have not shown that one can synthesize acarbose by expressing just one or more specific fragment of SEQ ID NO:7. On the same lines, applicants have also not shown that they were able to make acarbose by culturing host cells in which native genes involved in acarbose synthesis, if any, were fully eliminated or altered (again the scope of the term "altered": is also not clear). Applicants have not taught as to how such strains can function and produce acarbose without transforming them with vectors comprising all the acarbose synthesizing genes such as those present on SEQ ID NO:7. For the claimed methods to be enabled, there is a requirement of knowledge and guidance with regard to how such experiments can be performed. However, in this case the disclosure is limited to the production of acarbose from transformants cultured such that the transformed DNA comprising SEQ ID NO:7 is fully expressed and acarbose is produced. It would require undue experimentation of the skilled artisan to make and use the claimed acarbose with an undefined method (i.e., elimination of native genes or alteration of native genes etc.). The specification is limited to teaching use of SEQ ID NO: 7 or the minimum requirement of at least 3 genes (acbB,C,D) for acarbose synthesis but provides no guidance with regard to

the making of acarbose using any of the specific fragments of SEQ ID NO:7. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polynucleotide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by these claim.

The specification does not support the broad scope of the claims which encompass all above methods because the specification does not establish: (A) that one or more specific fragments can be successfully used for transformation and synthesis of acarbose; (B) a rational and predictable scheme for eliminating native acarbose genes with an expectation of obtaining the desired biological function; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, the claimed method of making acarbose is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action applicants have traversed the above rejection arguing that the specification on page 8, lines 2 and 3 refers to recombinant molecule to be used in acarbose production which comprises a DNA sequence depicted in figure 4 (i.e., SEQ ID NO:7) or parts thereof and that the specification teaches that not all of the genes are necessary for the biosynthesis of acarbose and that some regulatory genes can be deleted or modified. While it is agreed that the specification teaches the above, such a teaching does not provide guidance to those skilled in the art to practice what is claimed in the claims. For example where the specification teaches "or parts thereof", there is no explicit teaching that acarbose can be produced by eliminating or altering any or all parts of SEQ ID NO:7. Indeed specification teaches that specific parts are actually required and that not any or all parts of SEQ ID NO:7 can be eliminated. There is a minimum requirement of acbBCD genes for the host cells or natural cells to retain their ability to synthesis acarbose (see page 6 of specification).

Applicants also argue that pages 5-8 of the specification describes the six specific fragments of SEQ ID NO:7 that can be altered or eliminated, their encoded genes and their expected functions, such as biosynthesis of acarbose and that such genes may be eliminated by using vectors. Examiner respectfully disagrees that such a response would overcome the rejection. Pages 5-8 does describes the genes in SEQ ID NO:7. While applicants simply attribute the function as "bio-synthesis of acarbose", upon closer examination it will be revealed that each gene encodes polypeptides with specific activities such as aminotransferase, dTDP-glucose synthase, dehydratase activity etc. all of which may be required to act in concert towards the synthesis of acarbose. Specification is ambiguous as to which specific genes are essential for acarbose synthesis as it teaches at page 6, lines 12-15 that dTDP-glucose synthase and dTDP-

glucose 4,6-dehydratase "ought" to be involved in the biosynthesis of acarbose as opposed to a definitive teaching that it is indeed involved in acarbose synthesis. Therefore with such ambiguous teachings, those skilled in the art would be subject to undue experimentation to make and use the invention as claimed. Hence the rejection is maintained.

Conclusion

None of the claims are allowable.

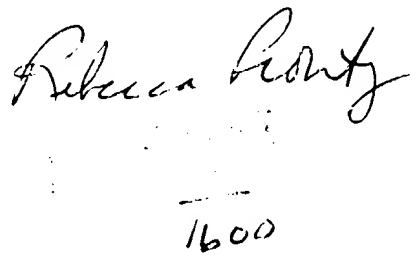
In view of the claim amendments, Examiner has withdrawn the rejection of claims 34-37 under 35 U.S.C. 112, Ist paragraph as lacking written description.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



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Manjunath N. Rao
November 19, 2003